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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,580	04/24/2001	Andrea Califano	YOR920000687US2	5406
7590	12/16/2003		EXAMINER	
Ryan, Mason & Lewis, LLP Suite 205 1300 Post Road Fairfield, CT 06430			CLOW, LORI A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/841,580	CALIFANO ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Lori A. Clow, Ph.D.	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 23 October 2003.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 1-28 is/are pending in the application.

4a) Of the above claim(s) 4-16,20-22 and 26-28 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-3,17-19 and 23-25 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
 a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) Notice of References Cited (PTO-892)      4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)      5) Notice of Informal Patent Application (PTO-152)  
 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.      6) Other: \_\_\_\_\_ .

## **DETAILED ACTION**

Applicant's election with traverse of the restriction requirement between Group I and Group II in the paper dated 23 October 2003 is acknowledged. The traversal is on the ground(s) that each Group is generally related to techniques for characterization of phenotypes and that a complete search would require a search of most, if not all, of the individual classes and subclasses. This is not found persuasive because as stated in the previous Office Action the method for transforming gene expression signals in Group I does not include the same steps as the methods for the characterization of phenotypes as in Group II. The search for the method steps of Group I would not necessarily result in those of Group II.

The requirement is still deemed proper and is therefore made FINAL.

### ***Specification Objections***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example page 26. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

*Non-Statutory Subject Matter*

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to **non-statutory subject matter**. The method to transform gene expression signals comprising determining the signals and deriving transformations using a function to create the transformation is only mathematical manipulation of the data generated from expression signals. A method which transforms gene expression signals to find certain patterns of expression **MAY** be one which produces a concrete, tangible, and useful result. However, some knowledge is required with regard to a specific patterns that result from such a method, for example. In the instant claims, there is no specificity identified as to what is intended by the outcome of the method. Therefore, the invention does not meet the standard of being immediately useful. Furthermore, there is no particular data identified or specific patterns recited in the specification such that a concrete, tangible, useful result is readily apparent. The specification is devoid of information on a possible correlation of this method to a particular disease or disorder for which this method may be useful or a particular phenotype, for example. There is no recitation of what to do with the probabilities generated or how that result of the method is concrete, tangible or useful.

As set forth in MPEP 2106: “For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See Alappat, 33 F.3d at 1543, 31 USPQ2d at 1556-57 (quoting Diamond v. Diehr, 450 U.S. at 192, 209 USPQ at 10). See also Alappat 33 F.3d at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) (“unpatentability of the principle does not defeat patentability of its practical applications”) (citing O’Reilly v. Morse, 56 U.S. (15 How.) at 114-19). A claim

is limited to a practical application when the method, as claimed, produces a concrete, tangible, and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible, and useful. See AT&T, 172 F.3d at 1358, 50 USPQ2d at 1452. Likewise, a machine claim is statutory when the machine, as claimed, produces a concrete, tangible, and useful result (as in State Street, 149 F.3d at 1373, 47 USPQ2d at 1601) and /or when a specific machine is being claimed (as in Alappat, 33 F.3d at 1544, 31 USPQ2d at 1557 (in banc).”

Furthermore, not all processes are statutory under 35 USC 101, as put forth in *Schrader*, 22 F.3d at 296, 30 USPQ2d at 1460. To be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technical arts is either disclosed in the specification or would have been known to the skilled artisan or (B) be limited to a practical application within the technological arts.

### *Utility*

Claims 1-3, 17-19, and 23-25 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims recite a method for transforming gene expression signals. The specification teaches that transformation of data can be used for identification of patterns in healthy versus unhealthy phenotypes such that these patterns may then be used to characterize an unknown sample into one of those two classes (page 6, lines 23-27; page 7, lines 1-2). However, the claimed method is not directed to the steps of classifying unknown samples into phenotype groups. It is merely directed to transforming data that represent gene expression signals. The specification does not teach any specific, substantial, or well-established utility for a method that simply transforms expression signal data. Use of the claimed method to analyze

the expression signals such that patterns are identified is certainly of scientific interest; however, no specific, substantial, and credible utility is set forth for the mere transformation of data as the “use” gained from this transformation is not disclosed or claimed. Utilities that require further research to identify or reasonably confirm a real-world context of use are not substantial utilities (See MPEP 2107.01). Therefore the claimed method does not have utility.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 17-19, and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 17, and 23 recite a method for transforming gene expression signals comprising “deriving a transformation that renders uniform, within a selected interval, a distribution of transformed gene expression signals for the gene”. It is unclear what is meant by a “transformation that renders uniform”. What is the definition of uniformity of a distribution? Is there a specific number that represents uniformity? What is the interval and is it selected based upon ranges of expression?

Claims 3, 19, and 25 recite, “using the function to create the transformation, wherein the transformation renders uniform a probability distribution”. It is unclear what is meant by rendering uniform a probability distribution. What are the parameters necessary to render a probability distribution uniform?

Claims 3, 19, and 25 recite, “wherein each gene expression signal is mapped by the transformation into a transformed gene expression signal”. Does applicant intend the transformation to actually map the signal? It is unclear what is meant by mapped. Is the signal physically mapped somewhere?

***Claim Rejections - 35 USC § 102***

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 17-19, and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eisen et al. (PNAS (1998) Vol. 95, pages 14863-14868).

In light of the 112, 2<sup>nd</sup> paragraph rejections above, the examiner is applying the prior art based upon the broadest possible interpretation of the claims.

The present claims are directed to a method, system, and article of manufacture for transforming gene expression signals by determining a plurality of expression signals, transforming the data, applying the transformation to other gene expression signals. The step of deriving a transformation includes transforming data such that a probability distribution is uniform and the signals are mapped.

Eisen et al. teach a system of cluster analysis for genome-wide expression data from DNA microarray hybridization (see abstract, column 1). Data are collected on spotted DNA microarrays and images are acquired for each fluorescence (signal). Intensity ratios are measured and master data tables are formed for all experiments. All ratios are then transformed to treat inductions or repressions of identical magnitude. Transformed data, equal to  $G_i$ , is used to gain a similarity score. A mean observation is gathered and standard deviations calculated such that a Pearson correlation coefficient of the X and Y observations is calculated, meeting the limitations of transformation and probability distributions page 14864, column 1). Furthermore, data are ordered such that they may be displayed. The display represents the ratio of gene expression levels as they show relationships among gene clusters.

While Eisen et al. do not use the specific algorithm, Splash, as disclosed in the specification, the claims do not require this algorithm. Therefore, it would have been *prima facie* obvious to one of skill in the art at the time of the invention to use the method of Eisen et al. in order to perform the steps of the method as claimed in the instant application. Eisen et al. motivates one to do so at page 14867, in stating:

This approach is a general one, with no inherent specificity to the particular method used to acquire data or even gene-expression data. It is therefore likely that similar approaches may be applied to many other kinds of very large data sets....We recognize that the particular clustering algorithm we used is not the only, or even the best, method available. We have used and are actively exploring alternatives such as parametric ordering and supervised clustering methods based on representative hand-picked or computer-generated expression profiles".

No claims are allowed.

### *Inquiries*

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

*Lori A. Clow*

**MARJORIE MORAN**  
PATENT EXAMINER

*Marjorie A. Moran*